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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/938,641	Applicant(s) MARX ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-17 and 19-38 is/are pending in the application.
- 4a) Of the above claim(s) 7-9,23-25 and 30-38 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,3-6,10,11,19,20,22 and 26 is/are allowed.
- 6) ☒ Claim(s) 13-17 and 27-29 is/are rejected.
- 7) ☒ Claim(s) 12 and 21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on October 6, 2003), Applicants filed an amendment and response received on January 6, 2004. Said amendment cancelled Claims 2 and 18 and amended Claims 5, 12-17, 22, and 27-28. Thus, Claims 1, 3-17, 19-38 are pending in the instant Office action.

Claims 7-9, 23-25, 30-38 remain withdrawn from consideration as non-elected invention(s). Claims 1, 3-6, 10-17, 19-22, and 26-29 will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of U.S. Provisional Application 60/279,415 filed on March 29, 2001 and foreign applications 10042052.4 and 10110053.1 filed in Germany on August 26, 2000 and March 2, 2001, respectively.

Certified translations of the foreign applications have been received; said applications support claims 1, 3-6, 10-17, 19-22, and 26-29, which are afforded an earliest effective filing date of August 26, 2000 in the instant Office action.

Information Disclosure Statement

3. The information disclosure statement filed on December 2, 2003, citing related applications, has been reviewed.

Withdrawn - Objections to the Specification

4. Previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicants' amendment.

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5. Previous objection to the specification for lacking updated U.S. patent application citations is withdrawn by virtue of Applicants' amendment.

Withdrawn - Objections to the Claims

6. Previous objection to Claims 2 and 18 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' cancellation of said claims.

7. Previous objection to Claims 5, 6, and 22 for using an improper genus/species name is withdrawn by virtue of Applicants' amendment. The Examiner notes that *Brevibacterium flavum* is also known as a *Corynebacterium*.

8. Previous objection to Claims 13-17 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicant's amendment rewriting said claims as independent claims.

Maintained – Objections to the Claims

9. Previous objection to Claim 12 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is maintained. Applicants argue that the amendment has obviated the rejection; the Examiner has carefully considered this argument, but disagrees.

As previously noted, "Claim 11 is drawn to SEQ ID NO:1, which is described as a DNA sequence – DNA being a double stranded molecule. Thus, a "complimentary" polynucleotide in no way further limits the DNA. For proper further limiting parameters, the claim must be drawn

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to a polynucleotide that is the full complement **of the coding strand** of SEQ ID NO:1”

(emphasis added). This amendment has not been made by Applicants. Correction is required.

10. Previous objection to Claims 21 and 27-28 for using an improper genus/species name is maintained. While Applicants corrected this error in an amendment to Claims 5, 6, and 22, no such amendment has been set forth for the instant claims. Applicants have noted that amendments have obviated the objections; the Examiner disagrees as evidenced by the maintenance of the instant objection. Correction is required.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

11. Previous rejection of Claims 2 and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “OxyR transcriptional regulator activity” is withdrawn by virtue of Applicants’ cancellation of said claims and by virtue of the presented articles that note the state of the art.

12. Previous rejection of Claims 6 and 22 under 35 U.S.C. § 112, second paragraph, as being indefinite for the species “*Brevibacterium lactofermentum*” and “*Brevibacterium divaricatum*” as synonyms for ---*Corynebacterium glutamicum*--- is withdrawn by virtue of Applicants’ amendment to said claims removing these redundant species synonyms.

13. Previous rejection of Claim 17 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “washing” as describing what is typically considered hybridizing conditions is withdrawn by virtue of Applicants’ amendment.

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14. Previous rejection of Claim 27 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase “enhanced expression of **the** *oxyR* gene” (emphasis added) is withdrawn by virtue of Applicant’s amendment to ---an overexpressed polynucleotide--- which clearly indicates any polynucleotide that meets the structural criteria noted in the claims and need not be endogenous to the coryneform cell.

15. Previous rejection of Claims 13-17 and 27 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants’ amendment to include structure and function in each claim.

16. Previous rejection of Claim 16 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants’ amendment limiting to a fragment of exact sequence.

Maintained - Claim Rejections - 35 U.S.C. § 112

17. Previous rejection of Claims 13-15 and 17 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for polynucleotides that encode SEQ ID NO:2, does not reasonably provide enablement for polynucleotides structurally related to SEQ ID NO:1, is maintained. Moreover, Claim 27 is added to the instant rejection based on the amendment by Applicants inserting previously rejected language. Applicants argue “pages 5-9 of the present specification provides copious amounts of guidance and definition to make and identify polynucleotides that fall within the scope”; the Examiner disagrees. The discussion of

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these pages is wholly generic to any polynucleotide encoding any protein and is not specific to a polynucleotide encoding oxyR. Moreover, this description, and the subsequent "isolation" of an oxyR gene, provides a skilled artisan with an ability to find other oxyR sequences, not with the ability to make as required by the statute.

18. Previous rejection of Claims 27-28 under 35 U.S.C. § 112, first paragraph, scope of enablement, amended herein based on the new limitation to overexpression in the claims and the definition of overexpression found in the specification.

Claims 27-28 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter wherein the promoter is responsible for the overexpression, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of

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experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the specification on page 9, means of overexpression are described. Said means include not only increasing the copy number of a gene or regulating the gene with a particular promoter, which means are enabled by the art, but also include altering the ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions, all of which are known in the art to "overexpress" a gene in specific examples, but none of which are predictable with oxyR or other genes that lack specific examples in the art. The specification provides no working examples or direction for overexpression using means of ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions. The nature of the invention is that these means are specific to a particular gene sequence and cannot be extrapolated from other, unrelated genes; there is no particular recipe of media that will overexpress all genes. Thus, overexpression using these methods is wholly unpredictable and not enabled by the specification or the art.

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19. Previous rejection of Claim 29 under 35 U.S.C. § 112, first paragraph, enabling deposit, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that a deposit receipt of DSM 13457, filed with the instant application, is sufficient to enable the claim. Firstly, the Examiner notes that no deposit receipt is found in the file. Secondly, the particulars of the deposit must be **amended into the specification** to enable the deposit. As previously noted, "to use the instant product, one of skill in the art is required to have DSM 13457 which is disclosed as *C. glutamicum* DSM5715 containing pT-oxyRexp. Thus, the plasmid or the description and availability of all its components for its construction must be publicly available. While the instant specification contains limited deposit information on page 6, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 13457, the following items are required: (1) the accession number assigned by the depository, (2) **the date of deposit**, (3) a brief description of the deposit, (4) the name and **full address** of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification)". Amendment to the specification and/or other enablement of the claimed host cell is required.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

20. Previous rejection of Claims 1-6, 10-22, and 26-28 under 35 U.S.C. § 102(a) as being anticipated by Nakagawa *et al.* is withdrawn by virtue of Applicants' filing of a translation of foreign priority documents.

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21. Previous rejection of Claim 16 under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession Number AE001274 is withdrawn by virtue of Applicants' amendment to closed language in the instant claim.

22. Previous rejection of Claim 17 under 35 U.S.C. § 102(b) as being anticipated by either GenBank Accession Number AF186371 or U18263 is withdrawn by virtue of Applicants' amendment requiring at least 70% sequence identity.

NEW ISSUES

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The inclusion of fragments of the complement of SEQ ID NO:1 is redundant because SEQ ID NO:1 is considered double stranded.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claim 16 is rejected under 35 U.S.C. § 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contains subject matter which

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was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Fragments of the non-coding polynucleotide portion of SEQ ID NO:1 5' to the coding sequence or 3' to the coding sequence, disclosed as 491-1471 in the sequence listing, are not supported by the specification as originally filed. Applicants are required to cancel the new matter or to cite clear support (page and line number) for the new matter in the specification as originally filed.

Summary of Pending Issues

25. The following is a summary of the issues pending in the instant Office action:

- a) Claim 12 stands objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.
- b) Claims 21 and 27-28 stand objected to for using an improper genus/species name.
- c) Claim 16 stands rejected under 35 U.S.C. § 112, second paragraph.
- d) Claim 16 is rejected under 35 U.S.C. § 112, first paragraph, new matter.
- e) Claims 13-15, 17, and 27 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement (breadth of structure/function).
- f) Claims 27-28 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement (overexpression).
- g) Claim 29 stands rejected under 35 U.S.C. § 112, first paragraph, enabling deposit.

Conclusion

26. Claims 1, 3-6, 10, 11, 19, 20, 22, and 26 are allowed. Claims 12 and 21 stand objected to and Claims 13-17 and 27-29 stand rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

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The instant Office action is **non-final** based on the new rejection concerning the enablement of "overexpression" as presented herein as based on the specification's definition of the term and not the art-defined meaning of the term.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Examiner
Art Unit 1652

March 23, 2004